



## The Effect of Diet, Lifestyle and/or Cognitive Interventions in Mild Cognitive Impairment: a Systematic Review

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### Background

As our population grows older, the risk of developing cognitive disorders increases and is a major public health challenge.<sup>1</sup> Mild Cognitive Impairment (MCI) is described as a transitional stage between the expected cognitive decline of normal ageing and that of dementia<sup>2</sup> and is suggested to be the optimum time point for preventative intervention<sup>3,4</sup>. Nutrition and cognitive decline has been examined in terms of a range of nutrients/dietary patterns, investigating the role that single nutrients, such as n-3 PUFA<sup>5</sup> as well as whole diet interventions, such as the DASH diet<sup>6</sup>, a ketogenic diet<sup>7</sup> or the Mediterranean diet<sup>8</sup> may have. Therefore, a rationale exists to systematically review the dietary intervention studies in the literature among this patient group.

### Objective

To examine the effect of diet, either alone or in combination with lifestyle and/or cognitive strategies, on cognitive health outcomes in patients with MCI.

### Methods

#### Inclusion Criteria

- Diagnosis of Mild Cognitive Impairment
- Community dwelling participants
- Randomised Controlled Trial

#### Exclusion Criteria

- Diagnosis of dementia or any other form of cognitive impairment other than MCI
- Participants with psychiatric problems e.g. depression or any significant medical comorbidity
- Individuals who are hospitalised, in a rehabilitation or long term care facility
- Pilot studies

#### Primary Outcome

- Incident Dementia/Alzheimer's Disease (AD)

#### Secondary Outcome

- Validated cognitive measure (neuropsychological and/or cognitive test)
- Data on quality of life, adverse events and biomarker analysis (e.g. structural MRI or amyloid imaging) if available

Database search: Ovid MEDLINE, EMBASE, PsycINFO, Web of science and Scopus

Records identified = 2130

Titles and abstracts screened = 1480

Full text articles screened = 33

Records after duplicates removed = 1480

Excluded = 1447

Studies included in analysis = 12

### Results

Reference	Intervention	Cognitive outcome measured
Ma (2016) <sup>10</sup>	Folic Acid (400 µg) (n=180, 6 months)	Memory*; Visuospatial skills*
de Jager (2012) <sup>11</sup>	0.8mg folic acid, 0.5mg vitamin B12, 20mg vitamin B6 (n=266, 2 years)	Memory*; Executive function*; Global cognition
Dekosky (2008) <sup>12</sup>	Ginkgo Biloba (120-mg) (n=482, 6.1 years)	Diagnosis of Dementia
Lee (2013) <sup>13</sup>	n-3 fatty acids (430 mg of DHA and 150 mg of EPA) (n=36, 12 months)	Memory*; Executive Function; Attention; Visuospatial Skills; Psychomotor speed; Global cognitive function
Petersen (2005) <sup>14</sup>	Vitamin E (2000 IU) (n=769, 3 years)	Development Alzheimer's disease; Memory; Executive Function; Language; Visuospatial skills; Overall Cognitive Function
Krikorian (2010) <sup>15</sup>	Chromium Picolinate (1000 mcg) (n=26, 12 weeks)	Memory; fMRI*
Desideri (2012) <sup>16</sup>	Cocoa Flavanols (990mg/520mg/45mg) (n=90, 8 weeks)	MMSE; Trail making test, Part A and B*; Verbal fluency test*
Krikorian (2010) <sup>17</sup>	Concord grape juice (n=12, 12 weeks)	Memory* (verbal learning only)
Krikorian (2010) <sup>18</sup>	Wild blueberry juice (n=9, 12 weeks)	Memory* (V-PAL test only)
Horie <sup>19</sup> (2016)	Nutritional counselling (healthy eating/calorie restriction) (n=80, 12 months)	Memory; Executive Function; Language; Psychomotor Speed
Bayer-Carter (2011) <sup>20</sup>	High-saturated fat/high-GI Vs low-saturated fat/low-GI diet (n=49, 4 weeks)	Memory; Executive Function; Motor Speed; AD Biomarkers* (CSF Aβ42 only)
Krikorian (2012) <sup>7</sup>	High carbohydrate Vs very low carbohydrate diet (n=23, 6 weeks)	Memory

\* indicates statistically significant difference between intervention and control/placebo at study completion (p<0.05)

### Discussion and Conclusion

Diet supplementation, with either Vitamin E<sup>14</sup> or Ginkgo Biloba<sup>12</sup>, had no statistically significant effect on progression from MCI to dementia and/or AD. There was heterogeneity in the results for cognitive function. Some studies showed improvements in a few of the cognitive tests used but not all, with some of the improvements observed not being maintained until intervention completion. The studies which investigated B vitamins and folic acid <sup>10,11</sup> and cocoa flavanols<sup>16</sup> showed the most consistent results in terms of cognition.

The mixed evidence may be explained by the heterogeneity of studies included, on the basis of:

- the variation in cognitive outcome measures used
- differences in the diet intervention type (supplements vs single food products vs dietary patterns)
- variations in sample size and duration of intervention
- the small number of dietary intervention studies conducted

These factors make it difficult to provide conclusive evidence to support the effect of diet on cognitive outcomes. Nonetheless, the review highlights the need for well-designed, robust RCTs to further explore the role of diet in cognitive decline.

<sup>1</sup>Peracino A and Pecorelli S. (2016) *Audiol Neurotol*, 21, 3-9.; <sup>2</sup>Roberts R and Knopman DS. (2013), *Clin Geriatr Med*, 29, 753-772.; <sup>3</sup>Voisin T, Touchon J. and Vellas B. (2003), *Curr Opin Neurol*, 16, 43-45.; <sup>4</sup>Massoud F, Belleville S, Bergman H *et al.* (2007) *Alzheimer's Dement*, 3, 283-291.; <sup>5</sup>Alles B, Samieri C, Feart, C *et al.* (2012), *Nutr Rev*, 25, 207-222.; <sup>6</sup>Smith PJ, Blumenthal JA, Babyak MA. (2010) *Hypertension*, 556, 1331-U85.; <sup>7</sup>Krikorian R, Shidler MD, Dangelo K *et al.* (2012), *Neurobiol Aging*, 33, 425.e19-425.e27. <sup>8</sup>Valls-Pedret C, Sala-Vila A, Serra-Mir M. (2015) *JAMA*, 175, 1094-1103.; <sup>9</sup>Moher D, Liberati A, Tetzlaff J. (2004) *PLOS*, 6, 1-6.; <sup>10</sup>Ma F, Wu T, Zhao J *et al.* (2016) *J Gerontol A Biol Sci Med Sci*, 1, 1376-1383.; <sup>11</sup>de Jager CA, Oulhaj A, Jacoby R *et al.* (2012) *Int J Geriatr Psychiatry*, 27, 592-600.; <sup>12</sup>DeKosky ST, Williamson JD, Fitzpatrick AL *et al.* (2008) *JAMA*, 300, 2253-2262.; <sup>13</sup>Lee LK, Shahar S, Chin AV *et al.* (2013) *Psychopharmacology*, 225, 605-612.; <sup>14</sup>Petersen RC, Thomas RG, Grundman M *et al.* (2005) *N Engl J Med*, 352, 2379-2388.; <sup>15</sup>Krikorian R, Eliassen JC, Boespflug EL *et al.* (2010) *Nutr. Neurosci*, 13, 116-122.; <sup>16</sup>Desideri G, Kwik-Urbe C, Grassi D *et al.* (2012) *Hypertension*, 60, 794-801.; <sup>17</sup>Krikorian R, Nash TA, Shidler MD *et al.* (2010) *Br J Nutr*, 103, 730-734.; <sup>18</sup>Krikorian R, Shidler MD, Nash TA *et al.* (2010) *J Agric Food Chem*, 58, 3996-4000.; <sup>19</sup>Horie NC, Serrao VT, Simon SS *et al.* (2016) *J Clin Endocrinol Metab*, 101, 1104-1112.; <sup>20</sup>Bayer-Carter JL, Green PS, Montine TJ *et al.* (2011) *Arch Neurol*, 68, 743-752.